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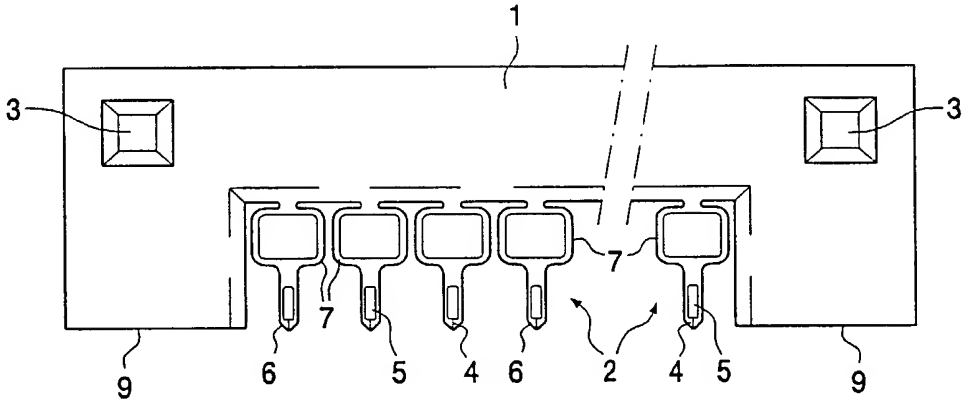
(54) Title: DEVICE FOR METERED COLLECTION AND DISPENSING OF LIQUIDS, METHOD FOR MANUFACTURING SUCH A DEVICE AND METHODS FOR COLLECTING AND DISPENSING LIQUIDS



(57) Abstract: The invention relates to a device for metered collection and dispensing of liquids, comprising: at least one metering element (2) for collecting and dispensing liquid, which metering element (2) is provided with at least one capillary channel (4), a holder for carrying the metering element, and a control system for controlling the position of the metering element. The invention also relates to a method for manufacturing such a device. The invention further relates to methods for collecting and dispensing liquids.

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DEVICE FOR METERED COLLECTION AND DISPENSING OF LIQUIDS, METHOD FOR MANUFACTURING SUCH A DEVICE AND METHODS FOR COLLECTING AND DISPENSING LIQUIDS

The invention relates to a device for metered collection and dispensing of liquids, comprising: at least one metering element for collecting and dispensing liquid, which metering element is provided with at least one capillary channel, a holder for carrying the metering element, and a control system for controlling the position of the metering element. The invention also relates to a method for manufacturing such a device. The invention further relates to methods for collecting and dispensing liquids.

Diverse types of metering elements for collecting and dispensing liquid are known in the prior art, such as pipettes, capillaries and syringes. Devices in which at least one of the above stated metering elements is incorporated are known from the patent publications US 4,003,262 and US 4,309,912. In addition to devices which include a single metering element, devices are also known in the prior art in which a plurality of metering elements are arranged, wherein the metering elements can be positioned one- or two-dimensionally relative to each other. Examples hereof are described in the patent publications US 4,276,048, GB 232 9599 and US 5,849,598. Devices which are provided with a plurality of metering elements usually have the characteristic of being mechanically complex. A drawback of the known metering elements is that they can only collect and/or dispense larger quantities of liquid in precise manner. Another drawback of the known metering elements is that a suction element frequently has to be coupled to the metering element, whereby liquid is drawn actively into the metering element. The patent publications NL 7802138 and US 4,152,939 describe respectively a rod or a needle as metering element, to which liquid 'adheres', mainly on a free outer end, as a result of binding cohesion forces. The advantage of the use of a needle or a rod is that, compared to the above stated metering elements such as pipettes, considerably smaller quantities of liquid can be collected and dispensed in metered manner. When precision mechanics are used to manufacture a needle or a rod, the smallest volume of liquid for metering has an order of magnitude of 10 nanolitres with a standard deviation of about 10%. A drawback of the known metering elements is that liquid volumes which are about a factor 100 smaller than the heretofore metered quantity of liquid of 10

nanolitres cannot be metered, while some (bio)chemical micro-analyses do require such 'pico'-doses.

The invention has for its object to provide a device with which it is possible to collect and dispense liquid in orders of magnitude of picolitres in metered manner while still retaining the advantages of the prior art.

The invention provides for this purpose a device of the type stated in the preamble, characterized in that the metering element is provided with an opening connected to the capillary channel for storing collected liquid, which opening is at least accessible from at least one direction perpendicular to the direction of transport of the liquid through the capillary channel. A first advantage of such a device is that liquid can be transported through the capillary channel as a result of a capillary action. Since no active suction elements are required for correct operation of the device, a passive suction of liquid occurs. The opening for storing collected liquid is preferably designed such that the drawn-up liquid can be held fast in controlled manner as a result of cohesion forces acting between the liquid and sides enclosing the opening. The relative positioning of the capillary channel and the opening for collecting liquid is co-determined by the production process of the device. Since known precision mechanics are unable to produce devices of very small size (or hardly so), with which liquid volumes in the order of magnitude of picolitres can be metered, the devices are preferably manufactured using etching techniques. Another significant advantage of the device according to the invention is that the mutual distance between two adjacent capillaries (also referred to as the "pitch") can be kept very small. Both the capillary channel and the opening can be manufactured in a single production run. If the properties of the liquid for drawing up are known, the control system can actuate the holder, and therefore also the metering element connected to the holder, such that a predetermined exact quantity of liquid can be collected or dispensed. Such devices can be applied particularly in (bio)chemical micro-analyses where an exactly determined 'pico-volume' of liquid is of great importance and wherein the positions for sampling are situated at very small mutual distances.

The opening is preferably dimensioned such that it is adapted to contain a liquid volume lying between 10 and 200 picolitres. Such small volumes for containing or storing liquid are not known in the prior art. As already described, the liquid collected by the device adheres to sides surrounding the opening owing to cohesive action. The quantity of liquid to be collected in the opening is so small that no droplet formation occurs in the liquid, thereby simplifying controlled collection and dispensing of liquid. Only part of the opening will generally be used to hold liquid.

The device is preferably provided with a plurality of metering elements which are arranged in a row, or one-dimensionally, relative to each other. This plurality of metering elements can be manufactured from a single material part (monolithic), for instance by means of making use of lithographic techniques which enable precise, controlled and very small mutual distances between the metering elements. A plurality of samples located at a very small mutual distance can thus be sampled simultaneously. In another preferred embodiment the device is provided with a plurality of metering elements which are arranged two-dimensionally (matrix or array form). Rows of the above discussed metering elements joined together in rows can be assembled for this purpose. This can be realized particularly accurately when the rows of metering elements manufactured from a single material part are also provided with fitting holes with which they are joined together.

The position of the metering element relative to the holder can preferably be changed. This can for instance be realized in that the metering element is connected to the holder via a support structure. When the holder is also provided with an aligning element for co-action with mating alignment means forming part of a metering element, rapid exchange of one or more metering elements then becomes relatively simple. The removed metering elements can be replaced by other metering elements. All metering elements (for instance a matrix) will generally be exchanged simultaneously. Multiple types of sampling can therefore be carried out using the same control system and holder.

The invention also provides a metering element for collecting and dispensing liquids, comprising: at least one capillary channel, and an opening connected to the capillary channel for storing collected liquid, which opening is at least accessible from at least one direction perpendicular to the direction of transport of the liquid through the capillary channel. The metering element preferably comprises a resilient element, which resilient element is deformable in a direction parallel to the capillary channel. A resilient suspension of the metering element is deemed of great importance, since the metering elements can hereby be brought into a certain contact with a surface when a plurality of metering elements are displaced simultaneously by a common carrier, even when the surface is not wholly flat. Damage to the metering elements can thus also be prevented.

The metering element is preferably manufactured from a single material part. Since the metering element is dimensioned such that a high accuracy and precision is required at the time of manufacture of the metering element, it can be advantageous or even necessary to manufacture the metering element integrally. Various aspects have already been described above with reference to the monolithic manufacture of a plurality of metering elements lying in a row. An example of a resilient element is an open ring shape, which in the loading situation can be compressed in radial direction. Such a resilient element can be manufactured by means of for instance etching technique/lithography simultaneously with etching of the capillary channel and the liquid holder.

The invention further provides an assembly of metering elements as described above, characterized in that a plurality of metering elements arranged in a row relative to each other are mutually connected via a support structure, and the metering elements and the support structure are manufactured from a single material part. The support structure is preferably provided herein with at least one opening adapted for co-action with an aligning element. A plurality of metering elements can thus be manufactured at a very short distance from each other and this furthermore only requires a single production run. Neither the very small mutual distance of the metering elements nor the accuracy of their mutual distance can be realized with the existing metering elements. In the case of

a plurality of support structures positioned relative to each other, these can be accurately positioned relative to each other in simple manner by means of the fitting openings.

The invention also provides a method for manufacturing an assembly of metering elements as described above by manufacturing a plurality of metering elements simultaneously from one material part by means of an etching technique, and a support structure such that the metering elements are connected to the support structure. The support structure is preferably provided with at least one (fitting) opening. The metering element can be manufactured from silicon or quartz. Quartz has the advantage of being obtainable in very pure form and being chemically relatively inert compared to other types of (at room temperature) solid materials, whereby the quartz is very suitable for analytic (bio)chemical applications. The metering element can also be manufactured from a silicon, for instance in the form of a wafer. The silicon is less chemically inert than the quartz and can therefore advantageously be provided with a coating, such as for instance a coating formed by polysilicon, silicon oxide, silicon nitride, teflon and so on. A coating has the advantage that the design freedom of the metering element is not limited in respect of for instance design, dimensions and production options, while a metering element with a relatively inert surface is still available.

In another preferred embodiment the metering element is manufactured using an etching and/or lithography technique. Such a production method has the advantage that metering elements provided with small openings and capillary channels can be manufactured with high precision, with which volumes of one or several picolitres can be metered and which can furthermore be accurately positioned at a small mutual distance.

The invention further provides a method for collecting liquid with such a device, comprising the following steps of: A) determining material properties of the bulk liquid for collection, B) inputting the material properties of the bulk liquid into the control system, C) causing the capillary channel of the metering element to make contact with the bulk liquid for a length of time determined by the control system, and D) ending the contact between the metering element and the bulk liquid. Inputting of the material

properties of the liquid into the control system enables the exact quantity of bulk liquid for collection to be related to the contact time of the metering element with the bulk liquid. Processing steps A) and B) can both be performed by the control system, whereby both processing steps can in fact be integrated into each other. The collecting of liquid using the device can also take place in non-controlled manner by immersing the openings connected to the capillary channels in the liquid. Although the collected volume of liquid is not known here, this nevertheless does not have to form a problem in metering controlled volumes of liquid. This is elucidated hereinbelow with reference to a method for metering liquid in controlled manner which also forms part of the present invention.

The invention further comprises a method for dispensing liquid with such a device, comprising the following steps of: A) determining material properties of the bulk liquid for collection, B) inputting the material properties of the bulk liquid into the control system, E) causing the capillary channel of the metering element to make contact with a delivery surface for a length of time determined by the control system, and F) ending the contact between the metering element and the delivery surface. Depending on the contact time of the metering element with the delivery surface, the liquid situated in the opening of the metering element can be delivered wholly or only partly to the delivery surface. In a preferred embodiment the processing steps C) and D) are carried out before processing steps E) and F) are performed. This method is applicable particularly advantageously when the delivery surface is manufactured from an absorbent material. The shape of a tip of a capillary channel and the surface area of such a tip can however also be indicative of a volume of liquid for metering.

The invention will be elucidated on the basis of non-limitative embodiments shown in the following figures, in which:
figure 1 shows a side view not to scale of a preferred embodiment of an assembly of a carrier and a plurality of metering elements connected to the carrier,
figure 2 shows a side view of the metering element according to figure 1, and

figure 3 shows a side view of the metering element according to figures 1-2 filled with liquid.

Figure 1 shows a preferred embodiment of an assembly of a carrier 1 manufactured from a single material part and a plurality of metering elements 2 connected to carrier 1. Carrier 1 is provided with two positioning openings 3, which positioning openings 3 serve as assist means in alignment of carrier 1 relative to other carriers 1 in order to thus form an accurate matrix of metering elements 2. Each metering element 2 is provided with a capillary channel 4 and an opening 5 connected to one side of capillary channel 4 for storing collected liquid. In the shown preferred embodiment the capillary channel 4 is positioned in or close to a point or tip 6 of metering element 2. Tip 6 is designed such that it tapers toward the free outer end. The free outer end of tip 6 can be given a wholly tapering form, but can also be provided with a truncated part of tip 6 positioned perpendicularly of capillary channel 4. A truncated part of the free outer end of tip 6 provides a certain degree of protection to capillary channel 4 during collection and/or dispensing of liquid, in that the truncated part functions as a stamp during collection and/or dispensing of liquid. Such a design also influences the quantity of liquid to be metered. Opening 5 is accessible on three sides. In addition to the access to opening 5 via capillary channel 4, opening 5 is also accessible from two directions which are perpendicular to the direction of transport of the liquid through capillary channel 4. Metering elements 2 are also provided with a resilient suspension construction 7 in the form of an open ring. The advantages of a resilient suspension construction have already been described above. Carrier 1 is further provided with stop surfaces 9 which define the maximum deformation of resilient suspension constructions 7. For a proper operation, a guaranteed contact with a delivery surface, the tips 6 of capillary channels 4 protrude beyond (in the figure below) stop surfaces 9 in the unloaded situation.

Figure 2 shows the metering element 2 according to figure 1. By means of capillary channel 4 liquid can be collected in opening 5 of metering element 2. It is also possible to fill opening 5 with liquid by immersing metering element 2 in a liquid. During contact of tip 6 with another object, for instance during collecting and/or dispensing of

liquid, a temporary deformation of suspension construction 7 ensures a correct positioning of tip 6 as well as an action damping the impact which occurs when contact is made between metering element 2 and the other object.

Figure 3 shows metering element 2 according to figures 1 and 2 filled with liquid 8. Opening 5 of metering element 2 is only partly filled with liquid 8. During contact of the free outer end of capillary channel 4 with a delivery surface (not shown) liquid 8 is displaced from opening 5 to the delivery surface. By coupling metering element 2 to a control system via carrier 1 the exact dosage volume can be determined and be related to the contact time of metering element 2 with a liquid or a delivery surface.

Claims

1. Device for metered collection and dispensing of liquids, comprising:
- at least one metering element for collecting and dispensing liquid, which metering element is provided with at least one capillary channel,
- a holder for carrying the metering element, and
- a control system for controlling the position of the metering element,
characterized in that the metering element is provided with an opening connected to the capillary channel for storing collected liquid, which opening is at least accessible from at least one direction perpendicular to the direction of transport of the liquid through the capillary channel.

2. Device as claimed in claim 1, **characterized in that** the opening is dimensioned such that it is adapted to contain a liquid volume lying between 10 and 200 picolitres.

3. Device as claimed in either of the foregoing claims, **characterized in that** the device is provided with a plurality of metering elements which are arranged in a row relative to other.

4. Device as claimed in any of the foregoing claims, **characterized in that** the device is provided with a plurality of metering elements which are arranged two-dimensionally relative to each other.

5. Device as claimed in any of the foregoing claims, **characterized in that** the metering element is releasably connected to the holder.

6. Device as claimed in any of the foregoing claims, **characterized in that** the metering element is connected to the holder via a support structure.

7. Device as claimed in any of the foregoing claims, **characterized in that** the holder is provided with an aligning element for co-action with mating alignment means forming part of a metering element.

8. Metering element for collecting and dispensing liquids, comprising: at least one capillary channel, and an opening connected to the capillary channel for storing collected liquid, which opening is at least accessible from at least one direction perpendicular to the direction of transport of the liquid through the capillary channel.

9. Metering element as claimed in claim 8, **characterized in that** the metering element comprises a resilient element, which resilient element is deformable in a direction parallel to the capillary channel.

10. Metering element as claimed in claim 8 or 9, **characterized in that** the metering element is manufactured from a single material part.

11. Assembly of metering elements as claimed in any of the claims 8-10, **characterized in that** a plurality of metering elements arranged in a row relative to each other are mutually connected via a support structure, and the metering elements and the support structure are manufactured from a single material part.

12. Assembly of metering elements as claimed in claim 11, **characterized in that** the support structure is provided with at least one opening adapted for co-action with an aligning element.

13. Method for manufacturing an assembly of metering elements as claimed in claim 11 or 12, by manufacturing a plurality of metering elements and a support structure simultaneously from one material part by means of an etching technique, such that the metering elements are connected to the support structure.

14. Method as claimed in claim 13, **characterized in that** the support structure is provided with at least one opening simultaneously with manufacture thereof.

15. Method as claimed in claim 13, **characterized in that** the metering elements are manufactured from silicon or quartz.

16. Method as claimed in any of the claims 13-15, **characterized in that** a layer of protective material is applied to the metering elements.

17. Method as claimed in any of the claims 13-16, **characterized in that** a lithographic treatment of a material part for processing takes place prior to performing the etching process.

18. Method for collecting liquid with a device as claimed in any of the claims 1-9, comprising the steps of:

A) determining material properties of the liquid for collection,

B) inputting the material properties of the liquid into the control system,

C) causing the capillary channel of the metering element to make contact with the bulk liquid for a length of time determined by the control system, and

D) ending the contact between the metering element and the bulk liquid.

19. Method for dispensing liquid with a device as claimed in any of the claims 1-9 and 18, comprising the steps of:

A) determining material properties of the liquid for collection,

B) inputting the material properties of the liquid into the control system,

E) causing the capillary channel of the metering element to make contact with a delivery surface for a length of time determined by the control system, and

F) ending the contact between the metering element and the delivery surface.

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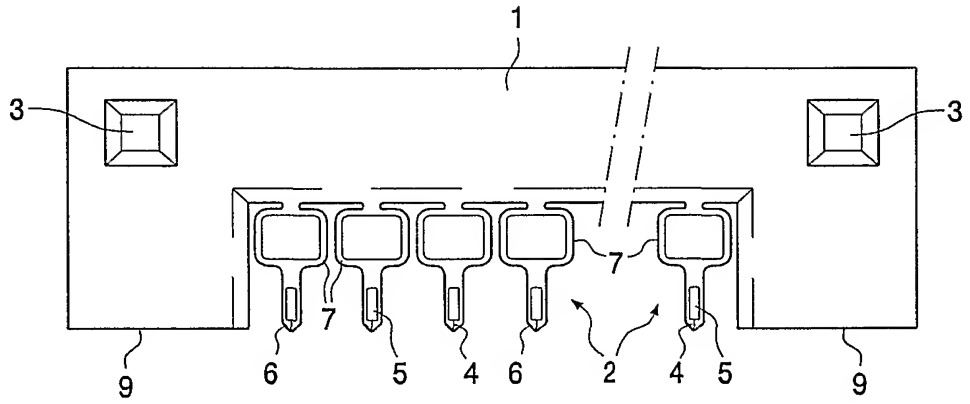

FIG. 1

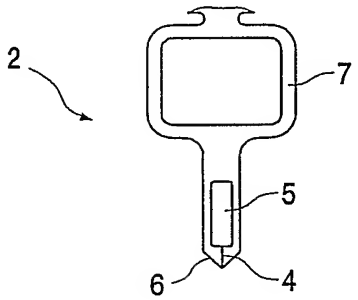

FIG. 2

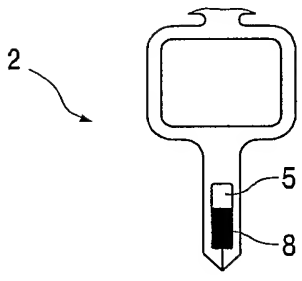

FIG. 3

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/02 G01N1/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 725 267 A (ROSSENDORF FORSCHZENT) 7 August 1996 (1996-08-07) column 2, line 10-44 column 4, line 1 -column 5, line 55; figures 2,5	1-19
X	US 5 957 167 A (FEYGIN ILYA) 28 September 1999 (1999-09-28) column 1, line 25 -column 2, line 65; figures	1-12,18, 19
Y	US 5 770 151 A (ROACH DAVID J ET AL) 23 June 1998 (1998-06-23) column 4, line 5 -column 5, line 7; figures	1-12,18, 19

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
7 November 2001	13/11/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Persichini, C

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL 01/00476

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	GB 2 211 111 A (SAXON MICRO LIMITED) 28 June 1989 (1989-06-28) page 1 -page 2; figures	1-12,18, 19

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

nformation on patent family members

Int ional Application No
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